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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,134	12/01/2003	Gary D. Niehaus	200047.150	6114

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EXAMINER

DO, PENSEE T

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/726,134

Applicant(s)

NIEHAUS ET AL.

Examiner

Pensee T. Do

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Withdrawn Rejection(s)

Rejection under 112, 1st paragraph in the previous office action is withdrawn herein.

Rejection under 102(e) by Anderson is withdrawn herein.

New Ground(s) of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 20 and 21 recite that the "substrate is positioned in the amount of liquid crystalline material so as to be ***movable throughout the liquid crystalline material***" (emphasis added). The present specification fails to teach that the substrate is within and movable throughout the liquid crystalline material. The specification, on page 26, lines 21-22, discloses that the "antibody coated microspheres is inserted into the lyotropic liquid crystal", but not that the coated microspheres (substrate) is movable within the liquid crystals.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear whether "ligands" in line 1, "a ligand" in line 4 and "one ligand" in line 7 are one ligand.

Claim 18 is indefinite for reciting "adapted to" in line 12. It is unclear how the ligand is modified to bind to the receptor.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claim 1 recites "a device for detecting ligands (hereon denoted as ligand 1)" comprising a substrate and at least one substrate attached to the substrate; wherein the receptor is capable of binding to **a ligand** (hereon denoted as ligand 1) to form a receptor-ligand complex; and wherein the substrate is positioned within an amount of liquid crystalline material having at least **one ligand** (hereon denoted as ligand 2) therein..." When all ligand 2 binds to the all receptors or takes up all the binding sites of the receptors bound to the **substrate within the liquid crystalline material**, binding of ligand 1 to the substrate within the liquid crystalline material is impossible because there

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is no more binding sites on the receptors attached to the substrate within the liquid crystalline material to accommodate ligand 1. Thus, **detection of ligand 1** is impossible. The device of claim 1 fails to establish a specific asserted utility of **detection of ligands or analyte of interest** (which might be in a sample) as recited in the preamble of claim 1.

Claims 1-17 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Maintained Rejection(s)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 9-11, 15-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of U.S. Patent No. 6,171,802 in view of Holmgren et al. (US 5,681,571).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 5 of patent '802 and the current invention are drawn to the same device for detecting ligands comprising multiple wells, the receptor is attached to the wells, wherein the receptor binds to the ligand and form a ligand-receptor complex which produces a signal; and an amplification mechanism, wherein said amplification mechanism is a lyotropic liquid crystalline material coupled to the receptor and said amplification mechanism amplifies said signal upon the formation of the ligand-receptor complex.

However, Patent '802 fails to teach the substrate which is made of polymers, such as polystyrene. Instead, Patent '802 teaches wells as substrate and the receptors are randomly distributed on those wells.

Holmgren teaches immunological assays using solid phase such as polystyrene microwells coated with receptor. (see col. 12, lines 38-44).

It would have obvious to one of ordinary skills in the art to use polystyrene microwell as a substrate as taught by Holmgren in the method of patent '802 since receptors can attach to those wells and must be randomly distributed on those wells. When the receptors are coated on the wells, coating must be done through physical or chemical attachment such as hydrophobic interactions and van der Waals interactions or covalent bonding respectively. Thus, one of ordinary skills in the art would be motivated to arrive at the present invention.

Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-6, 8-11, 15-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Abbott (US 6,284,197).

Abbott teaches a device and method for detecting analytes. The device comprises a substrate having a surface, the surface comprises a recognition moiety; a mesogenic layer/ liquid crystals oriented on the surface; and an interface between the mesogenic layer and a member selected from the group consisting of gases, liquids, solid and combination thereof. The interaction of the molecules with surface can be converted into an easily detected optical output. Abbott also teaches a method for detecting analytes comprising contacting with the analyte a recognition moiety for the analyte, wherein the contacting causes at least a portion of a plurality of mesogens/liquid crystals proximate to the recognition moiety to detectably switch from a

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first orientation to a second orientation upon contacting the analyte with the recognition moiety; and detecting the second configuration of the at least a portion of the plurality of mesogens, whereby the analyte is detected. The liquid crystals are used to amplify and transduce into an optical signal. The interaction of the liquid crystals with a surface can be converted into an easily detected optical output. Liquid crystal phase can be thermotropic or lyotropic. The recognition moieties are attached to the substrate surface through covalent bonding chemical interaction, ionic bonding, hydrophobic, van der Waals interactions, chemisorption, physisorption and combination thereof. The substrate surface can be made surface-active by attaching to the surface a spacer that has surfactant properties. Spacers serve to distant the recognition moiety from the substrate or self-assembled monolayer. Recognition moiety refers to molecules that are attached to either functionalized spacer arms or functionalized self-assembled monolayer components. The recognition moieties interact with analytes. The substrates can be inorganic crystals, inorganic glasses, metals such as gold, silver, platinum, palladium, nickel and copper, organic polymers such as polyethylene, polysobutene, polyacrylics, polystyrene, polyesters, polysulfones, etc. and combination thereof. Mesogenic layers have been anchored on curved surfaces. The local state of the mesogenic layer is similar to that of mesogenic layers anchored on a planar surface and properties of the mesogenic layer are not dominated by elastic energies caused by curvature. curvature. The receptor can be a monoclonal antibody.(col. 6, line 1-col. 6, line 30, col. 13, lines 12-17,. col. 14, lines 34-43, col. 35, lines 40-46).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 12-14 and 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abbott et al. (US 6,284,197) further in view of Tarcha et al. (US 5,252,459).

Abbott has been discussed above.

However, Abbott fails to teach that the shape of the substrate is spherical.

Tarcha teaches assay method using solid phase/substrate materials such as chromatographic, bibulous, porous capillary material, fiberglass, cellulose or nylon pad, silicon particles, porous gels such as silica gel, agarose, dextran, polyacrylamide beads, polystyrene beads, magnetic beads, etc. The method of attachment the specific binding member to the solid phase is by adsorption or covalent binding. (see col. 4, line 50-col. 5, line 17).

It would have been obvious to one of ordinary skills in the art to configure the shape of the substrate taught by Abbott into spherical shaped beads/particles as spherical shaped beads are well known in the art as solid phase supported by the teachings of Tarcha. Furthermore, since Abbott teaches that the properties of the mesogenic layer being anchored on a curved surface are the same as compared to those of the mesogenic layer when anchored on a planar surface, one of ordinary skills

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in the art would find it obvious to use substrate with a curved shape such as beads or particles.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Abbott (6,284,197) in view of Sahouani et al. (US 6,524,665).

Abbott has been discussed above.

However, Abbott fails to teach that the liquid crystalline material is chromonic.

Sahouani teaches an alignment structure useful in a liquid crystal display device comprising a substrate having disposed thereon a film of a lyotropic nematic or chromonic liquid crystalline material. Figure 1 in shows a scanning electron microscopic image of the surface of a polymeric substrate shear coated with a layer of compound A. (see col. 3, lines 5-11; col. 4, lines 65-69; col. 5, lines 1-4).

It would have been obvious to one of ordinary skills in the art to use chromonics as lyotropic liquid crystalline material in the method and device of Abbott because chromonic molecules show a self-organized surface structure that easily and uniformly orient liquid crystals or non-liquid crystal coatings in planar configuration. Thus, these self-organized surface structures can also easily and uniformly orient the receptors when become attached thereto. Such uniform orientation of the receptors would be an advantage because that way all receptors can be exposed to the ligands of interest and thus the signal would be accurate.

Response to Arguments

Applicant's arguments filed January 13, 2005 have been fully considered but they are not persuasive.

Regarding the double patenting rejection, Applicants argue that in light of the amended claims, the rejection of the Patent 6,171,802 in view of Holmgren no longer applies because the combination of the references do not teach a device wherein a substrate is positioned within an amount of crystalline materials forms a receptor-ligand complex.

The Patent '802 in view of Holmgren is still applicable to the amended claims which recites "the substrate is positioned within an amount of liquid crystalline materials" because the Patent '802 teaches that liquid crystalline material is coupled to the receptor which is attached to the well (substrate). Since the receptor is attached to the substrate, the substrate is covered by the receptor which is conjugated to a liquid crystalline material, the liquid crystalline material indirectly covers the well surface and thus the well (substrate) is partially within the liquid crystalline material.

Regarding the rejection under 102 by Abbott, Applicants argue that Abbott fails to teach that the substrate is within an amount of liquid crystalline material.

Abbott teaches a substrate having a surface, the surface comprises a recognition molecule (receptor), a mesogenic layer of liquid crystals oriented on the surface of the substrate. Apparently, the surface is covered with the liquid crystal materials, and thus the substrate is partially positioned within the liquid crystalline material. Thus, Abbott is indeed applicable to the amended claims.

Regarding the rejection under 103 by Abbott in view of Tarcha, Applicants argue that there is no teaching or motivation to combine the spherical particles of Tarcha with the method of detection as taught by Abbott. Furthermore, it would NOT be obvious to

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one of ordinary skill in the art to make the combination. The present invention is directed to the detection of ligand with high sensitivity, therefore, only small particles of ligand bound to the receptor are required to generate a signal. Tarcha teaches an indicator reagent formed by attaching an organic polymer particle to a binding member. However, Tarcha is not directed to a method of detection employing liquid crystals, and there is no teaching in Tarcha to place the spheres attached to the specific binding member into the liquid crystals to detect the presence of an analyte.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Tarcha is relied upon for the teaching of a polymeric spherical substrate. Thus, since Tarcha teaches a method of detection using a substrate and Abbott teaches a method of detection using a substrate, it would have been obvious to one of ordinary skills in the art to combine the references because Tarcha teaches that substrates can be in many shapes. Thus, using a variety of different shapes for the substrate brings more flexibility to the assay. Thus, any substrate that can bind a receptor would work in the method of Abbott, regardless of the shape. Tarcha needs not to teach a method of detection employing liquid crystals in order to have motivation to combine. If Tarcha taught a method of detection employing liquid crystals, then it would anticipate the present invention.

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Regarding the 103 rejection by Anderson or Abbott in view of Sahouani for claim 7, Applicants argue that there is no motivation to combine the references because such combination would not result in the present device according to claim 7, as neither Anderson or Abbott uses a receptor attached to a spherical particle that forms a receptor-ligand complex that alters the alignment of the liquid crystals, thereby producing an optical signal.

Claim 7 depends on claim 5 which depends on claim 1. All these claims do not recite a spherical substrate. Therefore, Anderson and Abbott do not need to teach a spherical particle.

Conclusion

Claims 20 and 21 are free of prior arts.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
March 21, 2005


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PRIMARY EXAMINER
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4/4/05